The Genetic Architecture of Hearing Impairment in Mice: Evidence for Frequency-Specific Genetic Determinants.

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Public Summary:
we have performed a comprehensive analysis in mice to elucidate the genetic architecture of hearing in response to tone burst stimuli. We identified multiple novel loci that are, for the most part, frequency-specific and illustrate the complex nature of mammalian hearing.

Scientific Abstract:
Genome-wide association studies (GWAS) have been successfully applied in humans for the study of many complex phenotypes. However, identification of the genetic determinants of hearing in adults has been hampered, in part, by the relative inability to control for environmental factors that might affect hearing throughout the lifetime, as well as a large degree of phenotypic heterogeneity. These and other factors have limited the number of large-scale studies performed in humans that have identified candidate genes that contribute to the etiology of this complex trait. To address these limitations, we performed a GWAS analysis using a set of inbred mouse strains from the Hybrid Mouse Diversity Panel. Among 99 strains characterized, we observed approximately two-fold to five-fold variation in hearing at six different frequencies, which are differentiated biologically from each other by the location in the cochlea where each frequency is registered. Among all frequencies tested, we identified a total of nine significant loci, several of which contained promising candidate genes for follow-up study. Taken together, our results indicate the existence of both genes that affect global cochlear function, as well as anatomical- and frequency-specific genes, and further demonstrate the complex nature of mammalian hearing variation.